

EXHIBIT M

Suture complications in a teaching institution among patients undergoing uterosacral ligament suspension with permanent braided suture

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Received: 20 November 2009 / Accepted: 10 January 2010 / Published online: 26 February 2010
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Abstract

Introduction and hypothesis Our study aimed to identify the rate of suture complications over a 5-year period using braided permanent suture for uterosacral ligament suspension (USLS) surgery.

Methods We reviewed the medical records of patients who underwent vaginal uterosacral ligament suspensions using braided polyester suture. Outcome measures included rate and timing of suture complications, patient symptoms post-operatively, efficacy of treatment modalities and surgical success.

Results Eighty-three patients had undergone USLS with braided, polyester suture over the study period that met inclusion criteria. Thirty-seven patients (44.6%) had suture-related complications post-operatively with a mean follow-up of 10.4 months. When only silver nitrate was applied, 16.7% improved, and when the suture was cut in clinic, 77.8% resolved.

Conclusions Permanent polyester braided suture for suspension of vaginal vault may lead to an unacceptably high suture erosion rate, cutting the suture in clinic results in the highest resolution.

Keywords Polyester suture · Suture complications · Uterosacral ligament suspension · Vaginal vault prolapse · Vault suspension

Abbreviations

USLS uterosacral ligament suspension

Introduction

Uterine and vaginal vault prolapse affects a large percentage of our aging population. Apical prolapse remains an important surgical challenge, with a significant percentage of patients requiring re-operation within a few years. Multiple surgical approaches, both vaginal and abdominal, have been used to treat this bothersome condition. More recently, mesh augmentation using pre-made kits have gained popularity for their ease and rapidity of placement. However, these techniques have not undergone rigorous study for short- and long-term complications. One popular approach to apical surgery is the uterosacral ligament suspension (USLS). It requires an intimate understanding of female pelvic anatomy and has been investigated by both retrospective and randomized studies. Researchers have found a 2–13% rate of recurrent vault prolapse. However, as with many surgical procedures, no uniform or standardized surgical approach has been established that improves outcome and reduces complications. No consensus exists on the types of sutures to use, how closely the sutures

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should be placed to the vaginal vault, or how many sutures should be placed on each side. Surgeons have reported using monofilament, delayed absorbable and permanent polyester sutures. Many believe that permanent suture will result in a more durable repair; however, no systematic comparisons have been made with other suture types. The aim of this study was to report the suture related complications in patients undergoing uterosacral ligament suspension with permanent braided polyester suture. Our secondary aim was to examine the rate of prolapse recurrence.

Materials and methods

We performed a retrospective cohort study of patients who underwent vaginal uterosacral ligament suspensions at Harbor UCLA Medical Center between March 2003 and March 2008. Institutional review board approval was obtained. All patients who had a vaginal approach were eligible for the study. Patients were excluded if they had abdominal or laparoscopic suspensions or had less than a 4-week follow-up. We gathered demographic data including age, parity, medical comorbidities, previous pelvic and urogynecologic procedures, and use of vaginal or oral estrogens from patient medical records. Intra-operative and post-operative complications, follow-up treatment, and post-operative prolapse recurrence and incontinence were abstracted from patient charts.

All patients underwent pre-operative pelvic examination. Pelvic organ prolapse was quantified using the Baden–Walker halfway system from 2003 to 2006 and the pelvic organ prolapse quantification system [1] from 2006 to 2008. Each subject underwent urodynamic assessment that included retrograde multichannel urethrocystometry, passive urethral pressure profilometry, cough and valsalva leak point pressures, simple uroflowmetry, post-void residual volume determination, and cystourethroscopy. Leak point pressures were evaluated both with and without prolapse reduced with two fox swabs to identify patients with occult incontinence.

Fellows and residents operated on patients in the Division of Pelvic Medicine and Reconstructive Surgery under the supervision of the two senior faculty members at our institution. Patients were given pre-operative antibiotics and sequential compression stockings for deep vein thrombosis prophylaxis. Once the hysterectomy with or without oophorectomy was performed, a moist laparotomy sponge was placed into the posterior cul-de-sac. Two Breisky–Navratil retractors were placed to protect the pelvic sidewall and help with visualization and palpation of the uterosacral ligament. The uterosacral ligament was identified and grasped 1 cm medial and posterior to the ischial spine with an allis clamp. A No. 0 permanent braided polyester suture (Ticron,

Tyco, Norwalk, CT, USA) was placed laterally to medially at this location and a second suture placed 1 cm cephalad to the first. This was repeated on the contralateral side. Once the sutures were secured, indigo carmine was injected intravascularly and cystoscopy performed. We placed lateral and medial tension on the suspension sutures while confirming bilateral ureteral efflux. Additional procedures were performed to repair defects in the anterior wall in a site-specific manner without the use of mesh. Patients who were identified with urodynamic stress or mixed incontinence underwent a sling procedure with Advantage* or Obtryx* (Boston Scientific Natwick, MA, USA) device using standardized techniques. After these procedures were performed, the USL sutures were attached sequentially to the anterior and posterior vaginal cuff while avoiding vaginal epithelium. Care was taken to stay 1 to 1.5 cm away from the outside margin of the cuff. The medial USL sutures were then tied before the lateral ones. Incontinence procedures and posterior compartment repairs were performed after repair of the anterior compartment, apical suspension procedure, and cuff closure, when appropriate. Irrigation was performed and the cuff was closed with interrupted No. 0 delayed absorbable sutures.

Patients were evaluated at 1 week, 6 weeks, 3 months, and 1 year. At each post-operative visit, patients were asked about incontinence, discharge, or bleeding. Suture erosion was defined as suture visible at the cuff greater than 6 weeks after surgery. Patients with suture-related complications underwent one of four possible treatments; observation, silver nitrate application, suture removal in clinic, or suture removal in the operating room. The type of treatment was based on clinician preference and severity of symptoms. Vaginal estrogen was given at the discretion of the physician. If outpatient interventions failed, the patient was ultimately taken to the operating room for suture removal and partial colpocleisis of the area of suture exposure.

Outcome measures included rate and timing of suture complications, patient symptoms, efficacy of treatment modalities, and surgical success. Recurrent prolapse was defined as Stage II or greater prolapse in any one compartment. We used basic descriptive statistics and chi-square analysis for evaluation of discrete variables. Data was analyzed using SigmaStat 3.5 (SigmaStat, Ashburn, VA, USA)

Results

Ninety-three patients underwent uterosacral ligament suspension with permanent braided, polyester suture over the 5-year study period. Four patients with abdominal USLS, three with laparoscopic USLS, and three patients with less than 4 weeks follow-up were excluded. The clinical and demographic characteristics of the 83 patients included in

the analysis are presented in Table 1. The mean (\pm standard deviation) age at surgery and mean parity of the 83 patients included in the analysis was 54.1 ± 9.9 (range 37–76) and 4 (range of 0–16), respectively. Approximately 56 (67.5%) patients were post-menopausal and 71.0% of our patient population was Hispanic. Eighty-one patients (97.6%) had a concurrent hysterectomy and 53 patients (63.9%) had anterior colporrhaphies. Mean blood loss was 301.5 cc (± 199). Median length of hospitalization was one day (mean 1.52, range 1–5, SD=0.088).

Peri-operative complications occurred in 19 patients (22.9%; Table 2). Surgical complications included blood loss requiring transfusion (two patients), fever [2], cuff abscess [1], and ureteral injury requiring stent placement [3]. Six (7.2%) additional patients had ureteral kinking identified during intra-operative cystoscopy and the offending suture was removed and replaced without further event. Post-operatively, two patients complained of buttock pain and three complained of leg numbness.

Two patients had new and ten patients had recurrent prolapse (14.5%) noted at their post-operative visit and none underwent repeat surgery at our institution. Mean follow-up was 10.4 months (range 1.13–62). The two patients with new prolapse had anterior vaginal wall prolapse and recurrent prolapse occurred in the anterior compartment (eight, 9.6%), posterior compartment (three, 3.6%), and apex in one patient (1.2%). Forty patients (48.2%) complained of stress incontinence symptoms pre-operatively, six of which had negative urodynamics and two who declined surgery. Patients who had concomitant slings with their prolapse repair had symptomatic improvement in their symptoms in 93.8% (30/32) of cases.

Thirty-seven patients (44.6%) had suture-related complications noted at their 6–8-week visit. Thirty of the 37

patients (36.1%) had suture exposure and seven patients (8.4%) were found to have only granulation tissue at the cuff. Patients with suture-related complications presented for routine follow-up with no symptoms (51.3%), vaginal bleeding (40.5%), and discharge (8.2%). In twenty-four patients, suture was visible by their 3-month visit (range 2.53–9.8; 64.9%).

At the time of this audit, 48.6% (18/37) had resolution of their suture-related complications and 19 patients did not. Of these 19 patients, 11 were lost to follow-up. Seven of the 11 patients who were lost to follow-up were asymptomatic (63.6%) at the time of their last visit. Seven of the total 37 patients had only granulation tissue noted, with three of these patients showing resolution (3/7=42%) after silver nitrate was applied, the other four did not return to clinic. Of the 30 patients with suture visible at the cuff, patients were either managed conservatively with observation, silver nitrate only, or silver nitrate and suture removal in clinic. Only one of six (16.7%) patients with suture visible at the vaginal cuff improved when only silver nitrate was applied and 77.8% resolved (7/9) when the suture was cut in clinic. Only 6/14 (42.8%) patients resolved when nothing was done ($p=0.36$). One additional patient had suture removed in the OR with resolution of her symptoms. Suture on average was cut 4.3 months after surgery (SD \pm 113 days). One patient had recurrent prolapse that had suture cut 1/10 (10%). These patients were followed on average 5.58 months (± 20.5) after the suture was cut.

Univariate analysis showed no increased risk of hypertension or diabetes in the group with suture complications. Also, menopausal status and age did not significantly impact suture complications and there was no statistically significant difference between patients with and without suture erosion ($p=0.2$ and $p=0.85$, respectively). There was no difference in patients who did and did not receive post-operative estrogen ($p=0.89$). Length of hospitalization did not differ in patients with (17 1 day, 19 greater than 1 day) and without suture complications (32 1 day, 15 greater than 1 day; $p=0.29$).

Type of concomitant procedure was not shown to impact development of suture complications. Patients undergoing posterior repairs ($p=0.89$), anterior repairs ($p=0.93$), slings ($p=0.46$), or patients undergoing more than three procedures at one time ($p=0.36$), did not show a difference in rate of suture complication (Table 3).

Discussion

Few studies have evaluated the most effective and safe suture for uterosacral ligament vault suspension (Table 4). Although performed for over 50 years, the technique has not been refined with robust comparative studies and most

Table 1 Summary data

Summary data	N
Cases	93
Excluded	10
Analyzed	83
Age (\pm SD)	54 (± 9.9)
Mean follow-up (range)	10.4 (1.1, 62 months)
Patients with prior surgery	2 (2.4%)
Patient with prior hysterectomy	2 (2.4%)
Post-menopausal (%)	56 (67.5%)
Ethnicity	
Hispanic	59 (71.0%)
Black	10 (12.0%)
White	7 (8.4%)
Asian	6 (7.2%)
Other	1 (1.2%)

Table 2 Pre-operative complications and outcomes

Complication	N (%)	Type	N (%)
Suture complications	37 patients (44.6%)	Visible suture at cuff	30 (36.1%)
		Granulation tissue only	7 (8.4%)
Post-operative prolapse	12 patients (14.5%)	Anterior compartment	8 (9.6%)
		Posterior compartment	3 (3.6%)
		Apical	1 (1.2%)
Other peri-operative complications	19 patients (22.9%)	Cuff abscess	1
		Transfusion	2 (2.4%)
		Fever	2 (2.4%)
		Buttock pain	2 (2.4%)
		Leg numbness	3 (3.6%)
		Ureteral kinking requiring stents	3 (3.6%)
		Ureteral kinking identified intra-op with resolution	6 (7.2%)

surgeons use clinical experience to guide their technique. In our study, there were a significant percentage of patients who developed either suture exposure or cuff granulation tissue post-operatively (44.6%) while using permanent braided suture. Two previous studies have evaluated the rate of suture complications in patients undergoing vaginal surgery with similarly high rates of erosion. Toglia [2] found that patients undergoing sacrospinous ligament suspension with the same suture had a 36% rate of suture complications. Seventy percent of symptomatic patients required suture removal and 74% presented with vaginal bleeding. Our patients also presented with vaginal bleeding and discharge and the most effective treatment ultimately was complete suture removal.

Luck et al. [3] also found a high rate of suture complications (31.3%) when using 2–0 permanent braided suture in posterior vaginal wall repairs, while only 9% had suture complications when using absorbable suture. In addition, patients who had sphincteroplasties at the time of surgery with permanent suture were at additional risk for wound breakdown and suture complications. They found that wound disruptions occurred earlier with absorbable suture (median 20 days) as compared to permanent suture

(median 53 days). Our findings, in addition to these published reports, add substantial evidence that the use of permanent braided suture at the suture line in vaginal procedures leads to bothersome symptoms and a high suture complication rate. Our paper reports suture complications in patients undergoing USLS procedures; however, as evidenced by these publications, permanent suture can cause problems in other types of vaginal procedures as well.

Other authors have reported outcomes from USLS procedures and type of suture used for these procedures varies widely. However, few have reported specifically on suture complications. Surgeons have used delayed absorbable [4–8], permanent monofilament [9] and permanent braided suture [10] with similar rate of recurrent prolapse. Aronson [11] was the only author who used braided suture and switched from 1–0 polyglycolic acid to monofilament polydioxanone during the study, however did not indicate a reason. This was presumably done for suture complications.

The reasons for suture complications are manifold. As the vaginal cuff is usually poorly vascularized post-surgically in post-menopausal women, there is a high risk of infection and healing problems. Foreign tissue reaction and chronic infection may lead to suture exposure and granulation tissue. Also, the cuff is often denuded of its peritoneum during hysterectomy and entrance into the pelvic cavity, which may impact wound healing. One option is to create clean margins by excising the cuff, prior to placing the sutures. Every effort should be taken by the surgeon to place the suture away from the cuff when passing through the posterior and anterior vaginal cuff. Ticon* is known for its tensile strength, but may have increased reactivity compared to monofilament suture such as polypropylene. It is likely that braided permanent suture inherently results in more suture complications in vaginal procedures, as compared to monofilament sutures. Some

Table 3 Concomitant procedures

Procedure	N	Percent
TVH	81	97.5
Anterior	53	63.9
With graft	7	8.4
Posterior	45	54.2
Anterior and posterior	27	32.5
Sling	31	37.3
BSO/USO	12	14.5

Table 4 Overview of uterosacral ligament vaginal vault suspension studies

Author	Type of suture	Suture placement	Complications	Cuff Closure/Cystoscopy	Success Rate
Amunsden et al. [7]	1 polyglactin or 0 polyglylconate	1st—at level of ischial spine; 2nd—more cephalad then first	1 transfusion	Not commented. Cystoscopy—before tying sutures	27/33 (82%) patient satisfaction; 94% objective cure
Aronson et al. [11]	1-0 braided polyglyactic acid, switched to 1-0 monofilament polydioxanone; 3 sutures bilaterally	Suture placed “deep” dorsally and posteriorly in the pelvis, through pararectal portion of ligament	24 (5.9%) blood transfusions; 2 partial SBO; 1 vaginal cuff abscess; 1 patient had ureteral injury	Not mentioned timing of cystoscopy or closure style	Not mentioned
Barber et al. [6]	Monofilament and 1–0 delayed absorbable monofilament; 2 sutures bilaterally	Sutures are placed at the level of ischial spine and 1 cm above	5/46 (11%) ureteral injury	Interrupted delayed absorbable; Cystoscopy after tying suture, but before attaching to cuff	90% objective
Jenkins [4]	1–0 delayed absorbable or monofilament; 2 sutures bilaterally	Placed into the medial/posterior/dorsal aspect of the USL; 2nd suture placed lateral to the first	3/50 (6%) suture erosion	Closed with delayed absorbable suture; Cystoscopy not performed	48/50 (96%). Failures were asymptomatic cystoceles
Karram et al. [5]	0 polypropylene; 2–4 bilaterally delayed absorbable to suspend cuff	USL palpated posterior and medial to ischial spine and placed above spine with polypropylene and delayed absorbable to suspend cuff	5/168 ureteral injury (2.4%); 1 small bowel injury; 1 pelvic abscess	Not discussed. Cystoscopy performed; uncertain timing	Patient satisfaction 150/168 (89%)
Schull et al. [10]	Non-absorbable braided; 3 sutures bilaterally	USL identified posterior and medial to ischial spines at 4 and 8 o’ clock. Needles passed lateral to medial	1% transfusion, 1% ureteral injury/kinking rate, and 0.3% post-operative death rate	Continuous delayed absorbable; cystoscopy—before and after tying suspensory sutures	251/289 (87%) objective
Silva et al. [8]	Same as Karram	Same as Karram	15.3% with surgical failure; no ureteral injuries	Not discussed; cystoscopy performed; uncertain timing	84.7% objective
Wheeler et al. [9]	Monofilament polypropylene; 1 suture bilaterally	Placed through the peritoneum and adjacent to the ligament 1 cm cephalad and at the same posterior level as the ischial spine	No ureteral injuries	Continuous running; cystoscopy after cuff closure	Patient satisfaction 88.9%

surgeons have even used polyglactin 910 suture with good results [2], claiming that scarring takes place that keeps the vault suspended as the suture breaks down [12]. Wheeler [9] chooses monofilament polypropylene sutures and places only one suture on each side and claims that this results in less devascularization at the vaginal cuff. After reviewing our own results, we have stopped using Ticron* suture and now all surgeons use polytrimethylene carbonate (Covidien synecture, Norwalk Connecticut) for vault suspension with good preliminary results.

There was also a significant risk of ureteral entrapment when the uterosacral ligament was suspended to the vaginal vault, as seen with previous studies [6, 11]. Six patients required release of the suture intra-operatively with no sequela and three patients required stent placement. No patients needed ureteral re-implantation or repair. Based on these findings, we have modified our technique, placing a single throw securing the uterosacral ligament prior to cystoscopy. We believe that simply placing tension on the sutures during cystoscopy may not completely occlude an entrapped ureter in some cases.

The strengths of this study included the large number of patients with suture complications, allowing a glimpse into the natural history of suture erosion and cuff complications with different treatment approaches. Visualized suture or granulation suture may resolve if seen immediately post-operatively, however those presenting greater than 3 months after surgery may require intervention and suture removal. A few patients were followed for almost 3 or 4 years, and their suture complications did not resolve without treatment. Physicians are often uncertain of the natural course of suture exposure. As suture exposures likely will not resolve with time, as evidenced by the majority of our patients needing suture removal, it is recommended to remove suture at the time of visualization. Chronic infection and granulation tissue formation will result in continued problems with bleeding and discomfort.

The weakness of this study was the retrospective design and the inconsistent patient follow-up. Since level of physician experience differed at the post-operative visit, recurrent vault prolapse may have been underestimated. It was also impossible to know why physicians chose a

certain intervention, and severity of findings or patient symptoms may have affected success of their intervention. A larger study size might have been able to identify differences between study groups in terms of age, blood loss, diabetes, and menopausal status. Our study was not powered to make meaningful analysis of these risk factors.

It is time to start fine-tuning our technique of surgical procedures like the uterosacral ligament that have been performed for decades. A randomized controlled trial that compares surgical techniques, suture type, and outcomes can greatly contribute to guiding surgeon practice. However, until such research is done, our study suggests that permanent braided suture should not be the first line material used in vaginal surgeries such as the uterosacral ligament suspension.

Acknowledgments There are no acknowledgments.

Conflicts of interest None.

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